

1/1 - (C) BIOSIS / BIOSIS XP-002176821
 AN - PREV199800350951
 TI - FK960, a novel potential anti-dementia drug, augments long-term potentiation in mossy fiber-CA3 pathway of guinea-pig hippocampal slices.
 AU - Matsuoka Nobuya; Satoh Masamichi
 AUAF- Div. Biological Sci., Exploratory Res. Lab., Tsukuba Res. Lab., Fujisawa Pharmaceutical, 5-2-3 Tokodai, Tsukuba, Ibaraki 300-2698; Japan
 PUB - Brain Research
 - June 1, 1998
 IRN - ISSN 0006-8993
 VOL - 794
 NR - 2
 PG - 248-254
 AB - Our previous studies have demonstrated that FK960 (FR59960; N-(4-acetyl-1-piperazinyl)-p-fluorobenzamide monohydrate), a novel antidementia piperazine derivative, exerts beneficial effects on memory deficits in various animal models of amnesia in rats (M. Yamazaki, N. Matsuoka, N. Maeda, Y. Ohkubo, I. Yamaguchi, FK960 N-(4-acetyl-1-piperazinyl)-p-fluorobenzamide monohydrate ameliorates the memory deficits in rats through a novel mechanism of action, J. Pharmacol. Exp. Ther., 279 (1996) 1157-1173.) and in rhesus monkeys (N. Matsuoka, T.G. Aigner, FK960 (N-(4-acetyl-1-piperazinyl)-p-fluorobenzamide monohydrate), a novel potential antidementia drug, improves visual recognition memory in rhesus monkeys: comparison with physostigmine, J. Pharmacol. Exp. Ther., 280 (1997) 1201-1209). To clarify the synaptic mechanisms of its anti-amnesic action, FK960 was investigated for its effects on the development of long-term potentiation (LTP) in guinea-pig hippocampal slices. The magnitude of LTP of population spike recorded in CA3 pyramidal neurons was significantly augmented by perfusing FK960 (10⁻⁹-10⁻⁶ M) for 25 min before and during tetanic stimulation of the mossy fibers, whereas the basal amplitude of population spikes before tetanus was hardly affected by the drug. The dose-response curve was bell-shaped with a maximal augmentation at 10⁻⁷ M. Scopolamine (10⁻⁶ M) per se had little effect on the magnitude of LTP in the mossy fiber-CA3 pathway, but significantly attenuated its enhancement by FK960 (10⁻⁷ M). In hippocampal slices from animals treated with cysteamine (200 mg/kg, s.c.), which was shown to deplete the hippocampal somatostatin, FK960 (10⁻⁷ M) hardly affected the LTP. These results suggest that FK960 enhances the magnitude of LTP in the mossy fiber-CA3 pathway through an activation of the cholinergic-somatostatinergic link in the hippocampal formation. Furthermore, it can be postulated that the drug regulates the cognitive function by modulating directly synaptic plasticity in the hippocampal neuronal network.